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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|----------------------------------------------------------------------------------------------------------------------|-------------|----------------------|---------------------|------------------|
| 10/584,960 | 11/04/2008 | David Threadgill | 421/99 PCT/US | 3931 |
| 25297 7590 01/19/2012 JENKINS, WILSON, TAYLOR & HUNT, P. A. 3100 Tower Blvd. Suite 1200 DURHAM, NC 27707 | | | | |
| EXAMINER DENT, ALANA HARRIS | | | | |
| ART UNIT | | PAPER NUMBER | | |
| 1643 | | | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary**Application No.**

10/584,960

Applicant(s)

THREADGILL ET AL.

Examiner

Alana Harris Dent, Ph.D.

Art Unit

1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 November 2011.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 5) ☒ Claim(s) 1-28 is/are pending in the application.
- 5a) Of the above claim(s) 13-28 is/are withdrawn from consideration.
- 6) ☐ Claim(s) ____ is/are allowed.
- 7) ☒ Claim(s) 1-12 is/are rejected.
- 8) ☐ Claim(s) ____ is/are objected to.
- 9) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 12) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-853)
Paper No(s)/Mail Date 07/31/06; 09/18/06
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date ____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: ____

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I (claims 1-12) in the reply filed on November 14, 2011 is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1-28 are pending.

Claims 13-28, drawn to non-elected inventions are not examined on the merits.

Claims 1-12 are examined on the merits.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greene et al./ U.S. Patent number 7,662,374 B2 (filed August 5, 2002), and further in view of Hallahan et al./ U.S. Patent application publication number US

2004/0191249 A1 (filed October 20, 2003). Greene teaches peptides of interest, such as members of the epidermal growth factor receptor EGFR (erbB1) family may be dimerized with each other to form homodimers, as well as heterodimers with other compounds, see column 5, lines 15-24; column 24, lines 4-9; and column 25, lines 5-30. Greene also teaches methods of making binding agents, such as antibodies which bind erbB receptors, see column 25, lines 31-55. Greene does not teach a method of screening a plurality of compounds implementing a phage-displayed antibody library comprising several solutions to select structures that do not contain any ERBB family members.

However, Hallahan teaches a method of screening a plurality of phage-displayed antibodies for an ability to bind to a target molecule present on a cell. In one embodiment, the method comprises contacting the cell with a first solution, the first solution comprising the plurality of phage-displayed antibodies; isolating a second solution, the second solution comprising those phage-displayed antibodies that do not bind to the cell; removing any phage-displayed antibodies bound to the cell; contacting the cell with the second solution; and (f) detecting binding of a phage-displayed antibody to the target molecule on the cell. In one embodiment, a phage-displayed antibody is a single chain fragment variable (scFv) antibody. In another embodiment, a phage-displayed antibody is an Fab antibody, see page 2, sections 0010 and 0011. Hallahan also teaches "[w]hen phage-displayed

antibodies bind to an antigen, they can be affinity-purified using the antigen. These affinity-purified phage can then be used to infect and introduce the antibody gene back into *E. coli*. The *E. coli* can then be grown and induced to express a soluble, non-phage-displayed, antigen-specific recombinant antibody. Phage display technology is especially useful for producing antibodies to antigens that are either poorly immunogenic or readily degraded and for which monoclonal and/or polyclonal antibodies are difficult to obtain...

Negative selection of phage can be first performed on a control tissue, for example untreated vascular endothelium. This can eliminate antibodies that nonspecifically bind...", see page 13, section 0137. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to screen for compounds that are able to bind EGFR/ERBB tumors using a phage-displayed library. The combination of positive and negative selection strategies and specific elution methods insures specific and selective binding, hence yielding molecules with increased affinity and avidity. These molecules will effectively bind their targeted receptors and may be used in method of treating EGFR/ERBB expressing tumors.

Conclusion

5. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana Harris Dent, Ph.D. whose telephone number is (571)272-0831. The Examiner works a **flexible schedule**, however she can generally be reached on 9 am to 6 pm, Monday through Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Misook Yu, Ph.D. can be reached on (571) 272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Art Unit: 1643

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Alana Harris Dent, Ph.D.

12 January 2012

/Alana Harris Dent, Ph.D./

Primary Examiner, Art Unit 1643